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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/928,326 | 08/13/2001 | Stephen Alistair Smith | P31831C1 | 7918 |

7590 07/25/2003

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| EXAMINER |
|---|
| CRIARES, THEODORE J |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/928,326 | SMITH, STEPHEN ALISTAIR | |
| | Examiner | Art Unit | |
| | Theodore J. Criares | 1617 | |

*-- Th MAILING DATE of this communication app ars on the cover sh t with th correspond nce address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

# ***CLAIMS 16-70 ARE PRESENTED FOR EXAMINATION***

*DETAILED ACTION*

Applicants claims are drawn to a method for the treatment of diabetes mellitus and conditions associated with diabetes mellitus which comprises administering 1-12 mg per day of 5-[4-{2-(N-methyl-N-(2-pyridyl)amino}benzyl]thiazolidine-2,4-dione (aka Rosiglitazone and BRL-49653) and an amount of insulin. The claims also claim a regiment of administering the combination on a daily dosage or twice daily.

Claims 33-35 are drawn to a method of treating diabetes mellitus by administering a combination of BRL-49653 and insulin.

Claims 16-32 are drawn to the treatment of diabetes mellitus with a combination of BRL-49653 and insulin wherein the amounts of BRL-49653 administered to a mammal is from 1-12 mg per day.

Claims 33 to 41 are drawn to various forms of the combination of BRL-49653 for administration with insulin.

Claims 43-70 are drawn to the treatment of diabetes Type II by administering BRL-49653 and insulin wherein the former is administered in anamount of from 1-12 mg. per day.

## ***Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieveley (6,153,632).

Rieveley teaches and claims, in the abstract, column 4, line 42 to column 7, line 42, and claims 15 and 24 the combination of BRL-49653 and insulin to treat diabetes mellitus and diabetes Type II. The amounts of BRL-49653 as claimed by the applicantin claims 16-32, 33-35 and 43-70 are obviated in under 35 U.S.C. 103(a) since claims 12-15 of the reference encompass the range of applicant's claims. Applicant's claims 25-31 et seq. are within this teaching since the range for administering the BRL-49653 with insulin is taught by Rieveley at column 4, lines 53 to column 5, line 35 to be from 1mcg to 10 grams. There is a lack of data or teaching in applicant's specification which indicates that the claimed range of from 1-12 mg. per day of applicant's claims is critical. Further there is a lack of teaching that the regimen of treatment of one to two times daily is critical as set forth in claims 25-41 and 63-70. See column 6, lines 40-61)

The formulation of BRL-49653 –maleate (claims 38-42) are obviated under 35 U.S.C. 103(a) since Hulin et al.(6,297,269) teach at column 12, line30-35 that insulin secretagogues, including BRL-49653, can form a salt with maleate. This reference further obviates claims 54-69 since at column13, lines 54-60 it is taught that the compounds of the invention include the hydrates thereof.

Claim 70 to a formulation of BRL-49653 in a microcrystalline is obviated under 35 U.S.C. 103(a) since one of ordinary skill in the art would be motivated, at the time of applicant's invention, to formulate BRL-49653 in a microcrystalline cellulose carrier

since Ikeda et al. (6,271,243) teach the formulation of Pioglitazone, a thiazolidinedione (as is BRL-49653), with said carrier at column16, Example 1.

None of the claims are allowed.

The test of obviousness is "whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 18 USPQ 2d 1885, (Fed. Cir. 1991). In view of the above rejection it is deemed that the evidence presented has established a prima facie case of obviousness.

None of the claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Theodore J. Criares whose telephone number is 308-

4607. The examiner can normally be reached on 6:30 A.M. to 5:00P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Theodore J. Criares can be reached on 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-6897 for regular communications and N/A for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1235.

Theodore J. Criares
Primary Examiner
Art Unit 1617

tjc
July 23, 2003